

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (currently amended): A method for optically detecting labeled molecules that have participated in a chemical reaction with a reagent supported on a surface and that have become temporarily supported at the site of the reagent, comprising:

- a) providing a flow cell;
- b) providing within said flow cell a solid support having a surface;
- c) supporting at least one reagent molecule to said surface;
- d) introducing two flowing solutions into said flow cell, wherein one of the two flowing solutions comprises a labeled molecule with a concentration above  $10^{-8}$  M that can contact said at least one reagent molecule, and one of the two flowing solutions comprises buffer with no detectable labels, and wherein the two flowing solutions are at different locations within the flow cell at any time;
- e) immersing the at least one reagent molecule in the flowing solution comprising a labeled molecule;
- f) switching or directing the two flowing solutions with respect to the at least one reagent molecule, or switching the location of the at least one reagent molecule with respect to the two flowing solutions, to immerse the at least one reagent molecule in the flowing solution comprising buffer with no detectable labels;
- g) providing a light source for illuminating an illumination zone within the flowing solution comprising buffer with no detectable labels;

- h) providing a detector for detecting light emitted from the illumination zone;
- i) substantially simultaneously to said switching or directing the two flowing solutions with respect to the at least one reagent molecule, or switching the location of the at least one reagent molecule with respect to the two flowing solutions, switching at least one of said light source, detector, or location of said at least one reagent molecule to cause the label of a labeled molecule which has reacted with said at least one reagent molecule to pass through said illumination zone; and
- j) detecting light emitted at said illumination zone to detect the presence of one or more labeled molecules,

wherein a series of chemical reactions is detected by repeating said steps of introducing the flowing solutions into said flow cell, immersing said at least one reagent molecule in the solution comprising labeled molecules, switching or directing the flowing solutions with respect to the at least one reagent molecule, or switching the location of the at least one reagent molecule with respect to the flowing solutions, switching at least one of said light source, detector, or location of said at least one reagent molecule to cause the label of a labeled molecule which has reacted with said at least one reagent molecule to pass through said illumination zone; and detecting light emitted at said illumination zone to detect the presence of one or more labeled molecules,

the time interval between successive chemical reactions controlled by controlling the time between successive repetitions.

Claim 2 (original): A method according to claim 1 wherein a single labeled molecule is detected by said step of detecting light emitted at said illumination zone.

Claim 3 (withdrawn): A method according to claim 1 wherein a chemical reaction is detected by detecting the presence of labeled molecules that have participated in said chemical reaction.

Claim 4 (original): A method according to claim 1 wherein a single chemical reaction is detected by detecting the presence of a single labeled molecule that has participated in said chemical reaction by said step of detecting light emitted at said illumination zone.

Claim 5 (withdrawn): A method according to claim 1 wherein the concentration of said labeled molecules is above  $10^{-8}$  M.

Claim 6 (withdrawn): A method according to claim 1 wherein the concentration of said labeled molecules is above  $10^{-7}$  M.

Claim 7 (withdrawn): A method according to claim 1 wherein the concentration of said labeled molecules is above  $10^{-6}$  M.

Claim 8 (withdrawn): A method according to claim 1 wherein the concentration of said labeled molecules is above  $10^{-5}$  M.

Claim 9 (original): A method according to claim 1 wherein the label is a fluorescent label.

Claim 10 (previously presented): A method according to claim 1 wherein the at least one reagent molecule is a complex comprising a surface-bound polymerase enzyme and a nucleic acid or a supported nucleic acid and a polymerase, and the solution of labeled reactive molecules comprises at least one type of fluorescently labeled NTP molecule with no quenching moiety.

Claim 11 (original): A method according to claim 10 wherein said fluorescent labels are attached to the beta or gamma phosphate of the NTP.

Claim 12 (original): A method according to claim 1 wherein two or more distinguishable types of labels are used to label two or more different types of reactive molecules.

Claim 13 (previously presented): A method of claim 1 wherein optical detection of the labels includes identifying the labels by a property selected from the group consisting of color of excitation light or emission light, fluorescence lifetime, fluorescence brightness, electrophoretic mobility, location of detection, and time of detection.

Claim 14 (currently amended): A method according to claim 3 1 wherein an array of supported reagents is used and wherein optical detection of the reactions ~~are~~ is separately accomplished for each reagent of the array.

Claim 15 (withdrawn): A method of claim 3 wherein a series of chemical reactions is detected by repeating said steps of introducing said at least two flowing solutions into said flow cell, immersing said at least one reagent molecule in the solution comprising labeled molecules, switching or directing the flowing solutions with respect to the at least one reagent molecule, or switching the location of the at least one reagent molecule with respect to the flowing solutions, switching at least one of said light source, detector, or location of said at least one reagent molecule to cause the label of a labeled molecule which has reacted with said at least one reagent molecule to pass through said illumination zone; and detecting light emitted at said illumination zone to detect the presence of one or more labeled molecules.

Claim 16 (withdrawn): A method of claim 15 wherein the time interval between successive chemical reactions is controlled by controlling the time between successive repetitions.

Claim 17 (withdrawn): A system for optically detecting the chemical reaction of a labeled molecule with a surface-bound reagent, wherein the chemical reaction involves at least one step in which the label of the labeled molecule is bound or stereo-chemically entrapped by the reagent, at least for a short interval of time  $t$  exceeding about 100 microseconds, comprising:

- a. a surface to which is bound a single reagent molecule, or an array of single reagent molecules at resolvable locations, said surface being contained within a flow cell;
- b. an illumination zone;
- c. a light source for illuminating said illumination zone;
- d. an optical detector for detecting light emitted by a label on said labeled molecule;
- e. at least two flowing solutions, wherein at least one solution comprises labeled molecules that can react with said surface-bound reagent, and at least one solution comprises buffer with no detectable label, and wherein the two solutions exist at distinct locations within said flow cell;

f. a means for switching at least one of the flow of said solutions, the physical location of the surface of said surface-bound reagent, to immerse the surface-bound reagent molecule in only one solution at a time;

g. a means for switching on and off at least one of the light source, the detection of light, or the relative location of the zone of illumination-and-detection and the surface of the surface-bound reagent, so that labels that pass nearby to the surface either pass through said zone or do not pass through said zone; and

h. a circuit for effectively synchronizing said illuminating said illumination zone with said switching at least one of the flow of said solutions or the physical location of the surface of said surface-bound reagent, to immerse the surface-bound reagent molecule in only one solution at a time.